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Chemical components of respirable particulate matter associated with emergency hospital admissions for type 2 diabetes mellitus in Hong Kong

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ABSTRACT

Background: Epidemiological studies have shown that short-term exposure to particulate matter (PM) mass is associated with diabetes morbidity and mortality, although inconsistencies still exist. Variation of chemical components in PM may have contributed to these inconsistencies. We hypothesize that certain components of respirable particulate matter (PM_{10}), not simply PM_{10} mass, can exacerbate symptoms or cause acute complications for type 2 diabetes mellitus (T2DM).

Methods: We used a Poisson time-series model to examine the association between 17 chemical components of PM_{10} and daily emergency hospital admissions for T2DM among residents aged 65 years or above from January 1998 to December 2007 in Hong Kong. We estimated excess risk (ER%) for T2DM hospitalizations per interquartile range (IQR) increment in chemical component concentrations of days at lag_0 through lag_3, and the moving average of the same-day and previous-day (lag_{0-1}) in single-pollutant models. To further evaluate the independent effects of chemical components on T2DM, we controlled for PM_{10} mass, major PM_{10} chemical components, and gaseous pollutants in two-pollutant models.

Results: In the single-pollutant models, PM_{10} components associated with T2DM admissions include: elemental carbon, organic carbon, nitrate, and nickel. The ER% estimates per IQR increment at lag_{0-1} for these four components were 3.79% (1.63, 5.95), 3.74% (0.83, 6.64), 4.58% (2.17, 6.99), and 1.91% (0.43, 3.38), respectively. Risk estimates for nitrate and elemental carbon were robust to adjustment for co-pollutant concentrations.

Conclusions: Short-term exposure to some PM_{10} chemical components such as nitrate and elemental carbon increases the risk of acute complications or exacerbation of symptoms for the T2DM patients. These findings may have potential biological and policy implications.

1. Introduction

The global diabetes epidemic is becoming a serious threat to public health. The first WHO Global Report on Diabetes showed that the number of people living with diabetes almost quadrupled to 422 million in 2014 from 108 million in 1980 (World Health Organization, 2016). This number is projected to be 592 million in 2038 (International Diabetes Federation, 2013). Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by high glucose levels in the blood caused by insulin resistance and relative insulin deficiency, accounting for >90% of all diabetes cases (American Diabetes Association, 2006).

The increase in diabetes prevalence in recent years may be primarily attributable to modern lifestyles including obesity, physical inactivity, and the growing aging population (Van Dieren et al., 2010). Both long-term (Anderson et al., 2012; Brook et al., 2013; Chen et al., 2016; Eze et al., 2014; Liu et al., 2016) and short-term exposure to (Goldberg et al., 2013; Kan et al., 2004) particulate matter (PM) have been linked to diabetes, although there are still inconsistencies among studies. For example, a 10 μg/m^3 increment in long-term fine particulate matter ($PM_{2.5}$) exposure was associated with 1.49 fold higher risk (95% CI, 1.37, 1.62) for diabetes-related mortality in the 1991 Canadian follow-up study (Brook et al., 2013), while the findings were negative in the American Cancer Society Cancer Prevention II study (Pope et al., 2004). Positive associations were reported for short-term PM_{10} exposure in Shanghai, China (Kan et al., 2004), but not in the ten metropolitan areas in the European Mediterranean region (Samoli et al., 2014).

The inconsistencies among previous studies might relate to numerous factors such as the population susceptibilities, diabetes prevalence,

Abbreviations: PM_{10}, particulate matter with aerodynamic diameter less than or equal to 10 μm; T2DM, type 2 diabetes mellitus; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; ICD-9, ninth revision of the international classification of diseases; OC, organic carbon; EC, elemental carbon; NO_3^-, nitrate; SO_4^{2-}, sulfate; NH_4^+, ammonium; Ni, nickel; Na^+, sodium ion; K^+, potassium ion; Cl^-, chloride ion; Al, aluminum; As, arsenic; Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Pb, lead.

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sample size, exposure assessment, and statistical methods in controlling for confounders. Another key factor is that PM composition may vary from location to location because PM is a mixture of different components associated with particular local and regional sources of air pollution.

Emergency hospital admissions for diabetes are due to acute complications of diabetes (e.g., ketoacidosis, hyperosmolarity) and acute onset of chronic complications (e.g., renal manifestations and peripheral circulatory disorders) (Amaize and Mistry, 2016). Time-series analysis is well suited for evaluating short-term effects of time-varying exposures on health. In the present study, we aimed to identify which chemical components of PM_{10} (PM with a diameter < 10 μm) are associated with T2DM emergency hospitalizations using 10 years of daily time-series data from January 1, 1998 to December 31, 2007 in Hong Kong.

2. Materials and methods

2.1. Air pollution and meteorological data

The Hong Kong Environmental Protection Department (HKEPD) established the PM_{10} chemical speciation network to measure twenty-six PM_{10} chemical components, in addition to PM_{10} mass. PM_{10} samples were collected with quartz filters using High Volume PM_{10} samplers. The filters were analyzed for gravimetric mass, elements (e.g., nickel, aluminum) by inductively coupled plasma atomic emission spectroscopy (ICP-AES), ions (e.g., sulfate, nitrate) by ion chromatography (IC), and elemental carbon/organic carbon by a thermal/optical transmittance method (Yuan et al., 2013). During the study period, 24-hour PM_{10} sampling was carried out at six air quality monitoring stations, these six monitoring stations interspersed in different districts of Hong Kong, which included Yuen Long, Tsuen Wan, Sham Shui Po, Tung Chung, Central Western, and Kwun Tong, and were reported to well represent the general population exposure on a regular basis (Fig. S1) (Pun et al., 2014b). After excluding those chemical components that had a contamination issue or that had >25% of samples below the analytical detection limit or that had >25% of missing values, in the end a total of 17 chemical components were retained for data analysis. They were elemental carbon (EC), organic carbon (OC), nitrate (NO_3^-), sulfate (SO_4^{2-}), ammonium ion (NH_4^+), chloride ion (Cl^-), sodium ion (Na^+), potassium ion (K^+), aluminum (Al), arsenic (As), calcium (Ca), cadmium (Cd), iron (Fe), magnesium (Mg), manganese (Mn), nickel (Ni), and lead (Pb). Nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3) were also monitored at the same day and the same monitoring stations with PM_{10} chemical components. Air pollutant concentrations generally had moderate-to-very high monitor-to-monitor correlations (Table S1). We also obtained daily mean temperature and relative humidity data from the Hong Kong Observatory for the same study period.

2.2. Type 2 diabetes mellitus hospitalizations

We computed daily counts of emergency hospital admissions for the elderly aged 65 years or older with the principal diagnosis of T2DM [International Classification of Diseases, 9th revision (ICD-9): 250.X0 and 250.X2, X = 0–9] recorded in the Hospital Authority Corporate Data Warehouse, which covers all publicly funded hospitals that provides 24-hour accident and emergency services and covers 90% of hospital beds for Hong Kong residents (Tian et al., 2016). The Accident and Emergency (A&E) Departments in all publicly funded hospitals of Hong Kong adopted a triage system to ensure that patients with more serious conditions were accorded higher priority in medical treatment (Ho, 2013). Patients who did not require emergency attendance would not be treated in A&E Department but rather transferred to public or private clinics. The diabetes patients included in the current study were those with acute complications or with acute symptoms related to chronic conditions.

2.3. Statistical analysis

PM_{10} samples were collected on average every-sixth-day on a distinct sampling schedule for each of the six monitoring stations, thus for one particular day, there may be zero or multiple samples taken from the whole territory. Collectively, 69% of the study days had speciation measurements from at least one station; there is not an obvious pattern for missing data occurrence in the time-series. To compute the territory-wide mean concentrations of PM_{10} chemical components, we applied a centering method to remove the station-specific influence on the measurements of each component. Details of the centering method were reported elsewhere (Katsouyanni et al., 1996; Pun et al., 2014a; Wong et al., 2001). Fig. S2 shows time-series plots of PM_{10} chemical components. All pollutant concentrations are expressed in $\mu g/m^3$ except for EC and OC, which are reported in μg carbon/m^3.

This was a time-series study, and we used generalized additive models to estimate associations between PM_{10} chemical components and emergency hospital admissions for T2DM. The same-day mean temperature ($Tmean_0$) was used to control for the immediate effect of temperature, while the moving average of lag 1–3 days ($Tmean_{1-3}$) was used to control for the delayed effects of temperature. Natural cubic splines with 8 degrees of freedom (*df*) per year were used to control for time trend and seasonality. We used natural cubic splines with 3 *df* for both $Tmean_0$ and $Tmean_{1-3}$ to account for the nonlinearity of temperature effect, and included them simultaneously in the model (Tian et al., 2014). We used natural cubic spline with 3 *df* to control for the same-day mean relative humidity (*rh*). We also adjusted for day of the week (*DOW*), public holidays (*Holiday*), and influenza epidemics (*influenza*) as dummy variables. Our model is shown as follows:

$$\begin{aligned}\log[EY] = {} & \mu + \beta_1 COMP + ns(time, df = 8/\text{year} \times no.\text{of year}) \\ & + ns(Tmean_0, df = 3) + ns(Tmean_{1-3}, df = 3) \\ & + ns(rh, df = 3) + \beta_2 DOW + \beta_3 influenza + \beta_4 Holiday\end{aligned} \quad (1)$$

where *COMP* represents PM_{10} chemical components, *ns*(.) denotes natural cubic splines, and β_i indicates regression coefficients.

We first used single-pollutant models to examine the association of emergency hospitalizations for T2DM with each PM_{10} component on the same day (lag_0) and the previous 1–3 days (lag_1 to lag_3), and the moving average of same-day and previous-day (lag_{0-1}) while adjusting for time-varying confounders. For chemical components demonstrating statistically significant associations at lag_{0-1} in single-pollutant models, we further constructed two-pollutant models. We adjusted one at a time for PM_{10} mass, the major PM_{10} components (those contributing ≥4% to PM_{10} mass: EC, OC, SO_4^{2-}, NO_3^-, and NH_4^+), and gaseous pollutants (SO_2, NO_2, and O_3). Risk estimates were treated with caution when correlation between the two pollutants was ≥0.6 (Bell et al., 2014; Mostofsky et al., 2012; Tian et al., 2013). Besides that, we also included Ni which was significantly associated with diabetes hospitalizations in the single-pollutant models. For sensitivity analysis, we reanalyzed the time-series data using linear interpolation to fill in missing data for the days without data from any stations via the *na.approx* function in the R *zoo* package (Pun et al., 2015; Pun et al., 2014b).

The results were reported in terms of the percentage excess risk (ER%) increase in daily T2DM emergency hospitalizations for an interquartile range (IQR) increment of PM_{10} chemical components, and respective 95% confidence intervals (CI). All statistical significance tests were two-sided, and values of $p < 0.05$ were considered statistically significant. The data were analyzed using the statistical software R (version 3.1.2), and the "mgcv" (version 1.8–12) package.

3. Results

During the 10-year study period of 3652 days, we identified 40,150 T2DM emergency admissions (11.0 ± 3.8 admissions per day), with a mean age of 76 (range: 65–104) and female percentage 57.4%. Among